



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,168	02/07/2001	David J. Wright	P-4423D1	8991

26253 7590 09/02/2005

DAVID W. HIGHET, VP AND CHIEF IP COUNSEL
BECTON, DICKINSON AND COMPANY
1 BECTON DRIVE, MC 110
FRANKLIN LAKES, NJ 07417-1880

EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
----------	--------------

1634

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/778,168

Applicant(s)

WRIGHT ET AL.

Examiner

BJ Forman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-19,21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-19,21 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 June 2005 has been entered.

Status of the Claims

2. This action is in response to papers filed 29 June 2005 on which an RCE was filed and the previous rejections were traversed. The previous rejections under 35 U.S.C. 103(a) are withdrawn maintained. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Claims 1, 3-19 and 21-22 are under prosecution.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1634

4. Claims 1, 3-5, 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996) in view of Lee et al (U.S. Patent No. 6,207,379, filed 11 September 1998) and Fauser et al (BioTechniques, 1997, 22(5): 964-968).

Regarding Claim 1, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. β^+ vs β^s , Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54). While the method steps do not require isothermal amplification, Caskey et al teach the amplification via hybridization and primer extension (as claimed) wherein the extension utilizes known a polymerase e.g. Taq or DNA polymerase (Klenow) at a temperatures of 8-90 °C (Column 8, lines 21-26). This clearly suggests isothermal amplification. Furthermore, Lee et al teaches a similar method of diagnostic primer amplification wherein the amplification is performed under isothermal conditions (i.e. at the melting temperature of the template) whereby primer is rapidly hybridized to and denatured from the target (Column 7, lines 53-60). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the isothermal amplification of Lee et al to the amplification of Caskey et al based on Caskey's suggestion to do so. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the benefits taught by Lee et al primer is rapidly hybridized to and denatured from the target (Column 7, lines 53-60).

Caskey et al teaches diagnostic nucleotide 5 nucleotides from the 3' terminal, they do not teach 2 to 4 nucleotides from the 3' end. However, diagnostic nucleotides 2 to 4 nucleotides from the 3' nucleotide were known in the art as taught by Fauser et al (page 966,

Art Unit: 1634

Table 1). Fauser et al further teach these primers improve allele-specificity (page 965, lines 1-4). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to re-position the diagnostic nucleotide of Caskey et al to a position between 2 to 4 bases of the 3' nucleotide as taught by Caskey et al for the expected benefit of improved allele specificity as taught by Fauser et al (page 965, lines 1-4). One of ordinary skill in the art would have been further motivated to re-position the diagnostic nucleotide using routine experimentation to optimize allele-specific primers.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 3, Caskey et al teach the method using multiple detector primers, each comprising different diagnostic nucleotides (e.g. M vs S or Z, Example 4).

Regarding Claim 4, Caskey et al teach the method wherein the two primers are used to identify which of two possible SNP is present (e.g. M vs S or Z, Example 4).

Regarding Claim 5, Caskey et al teach the method wherein four detector primers are used (e.g. M (1) vs Z (2) and M (3) vs S (4), Example 4).

Regarding Claim 7, Caskey et al teach the method wherein detector primers have a non-diagnostic mismatch (Column 5, lines 20-46).

Regarding Claim 8, Caskey et al teach the method wherein the non-diagnostic nucleotide is within 15 nucleotides of the detector nucleotide i.e. the primers are preferably 12-16 (Column 4, lines 39-40). Hence, the non-diagnostic nucleotide is within 15 as claimed.

Regarding Claims 9-10, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the

Art Unit: 1634

efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. β^+ vs β^s , Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54).

Caskey et al further teach detector primers having non-diagnostic mismatch nucleotides whereby the more perfectly matched primer will be favored in the amplification reaction (Column 5, lines 20-46). Caskey et al also teach the primers are preferably 12-16 (Column 4, lines 39-40) and they illustrate diagnostic nucleotides positioned 5 bases from the terminal nucleotide (Examples 3-4). They do not specifically teach the non-diagnostic nucleotide 5 nucleotides from or adjacent to the diagnostic nucleotide. However, the addition of a non-diagnostic nucleotide (as they clearly suggest) to their exemplified 12 nucleotide primers would position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide. Hence, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add a non-diagnostic nucleotide to the diagnostic primer of Caskey and to position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide based on the available nucleotide positions within the 12 nucleotide primers exemplified by Caskey et al.

Regarding Claim 11, Caskey et al teach the method wherein the detector primer is 15-36 nucleotides (Column 4, lines 37-41).

Regarding Claim 12, Caskey et al teach the method wherein the detector primer is 18-24 nucleotides (Column 4, lines 37-41).

Regarding Claim 13, Caskey et al teach the method wherein the amplification is nucleic acid based amplification (Column 7, lines 31-50).

Regarding Claim 14, Caskey et al teach the method wherein the detector primer is 12-50 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 15, Caskey et al teach the method wherein the detector primer is 12-24 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Art Unit: 1634

Regarding Claim 16, Caskey et al teach the method wherein the detector primer is 12-19 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 17, Caskey et al teach the method wherein the SNP is detected by means of a label attached to the primer (Column 6, lines 16-35).

5. Claims 6 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996) in view of Fauser et al (BioTechniques, 1997, 22(5): 964-968) as applied to Claim 1 above and further in view of Whitcombe et al (U.S. Patent No. 6,326,145, filed 25 November 1998).

Regarding Claims 6 and 18-22, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. $\beta+$ vs β^s , Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54).

Caskey et al also teach primers labeled using art recognized techniques (Column 6, lines 16-35) but they do not teach tailed primers, primers detectable upon extension, primers labeled with donor/quencher dyes, quantitatively detected and displaced by an upstream primer.

However, these elements were well known in the art at the time the claimed invention was made as taught by Whitcombe et al (Column 4, lines 31-65) wherein binding results in abolished signal (Column 4, lines 49-53). Whitcombe et al further teach their method is useful

Art Unit: 1634

for strand displacement (Column 5, lines 57-59) and especially quantitative allele discrimination (Column 6, lines 33-43 and Column 10, line 60-Column 11, line 17).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the tailed primers having donor/quencher dye attached as taught by Whitcombe et al to the allele-specific primers of Caskey et al for the expected benefit of providing quantitative analysis of clinically important nucleic acids e.g. HIV nucleic acids as taught by Whitcombe et al (Column 6, lines 33-43).

Response to Arguments

6. Applicant asserts that Caskey et al do not specifically teach isothermal amplification as claimed. The argument has been considered but is deemed moot in view of the new grounds of rejection above.

Applicant asserts that Kwok et al teaches away from the instant invention because they teach that a single mismatch 3 residues has no significant effect on PCR product yield. The argument has been considered but is not found persuasive because the instant claims are drawn to isothermal amplification, not PCR. Therefore, the arguments are not commensurate in scope with the claims.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Art Unit: 1634

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 3-19 and 21-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 13-14, 16-17 and 19-23 of copending Application No. 10/202,896. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to method for detecting a single nucleotide difference in target nucleic acids and differ only in the arrangement of the limitations within the claim sets. For example, instant Claim 1 defines the detector primer as having a diagnostic nucleotide two to four nucleotides 5' of the 3' nucleotide while dependent claim 7 defines the '896 diagnostic nucleotide as N-1 to N-4. As such the claim sets are drawn to methods that are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

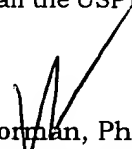
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Art Unit: 1634

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
August 30, 2005